WHAT IS CLAIMED IS:

1. A method for identifying a compound that modulates animalia tRNA splicing endonuclease activity, said method comprising:

(a) expressing a nucleic acid comprising a reporter gene in a cell, wherein the reporter gene comprises a tRNA intron;

(b) contacting said cell with a member of a library of compounds; and

(c) detecting the expression of said reporter gene, wherein a compound that modulates tRNA splicing endonuclease activity is identified if the expression of said reporter gene in the presence of a compound is altered relative to the expression of said reporter gene in the absence of the compound or the presence of a control.

2. A method for identifying a compound that modulates animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting a member of a library of compounds with a cell-free extract and a nucleic acid comprising a reporter gene, wherein the reporter gene comprises a tRNA intron; and

(b) detecting the expression of said reporter gene, wherein a compound that modulates tRNA splicing endonuclease activity is identified if the expression of said reporter gene in the presence of a compound is altered relative to the expression of said reporter gene in the absence of said compound or the presence of a control.

3. A method for identifying a compound that modulates animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting a member of a library of compounds with a cell containing a nucleic acid comprising a reporter gene, wherein the reporter gene comprises a tRNA intron; and

(b) detecting the expression of said reporter gene, wherein a compound that modulates tRNA splicing endonuclease activity is identified if the expression of said reporter gene in the presence of a compound is altered relative to the expression of said reporter gene in the absence of said compound or the presence of a control.

4. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) microinjecting a substrate of a tRNA splicing endonuclease into a animalia cell, wherein the substrate is labeled at the 5' end with a fluorophore and at the 3' end with a quencher;

(b) contacting the cell with a member of a library of compounds; and

(c) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if a fluorescent signal is not detectable or decreased in the presence of the compound relative to the absence of the compound or the presence of a control.

5. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) transfecting a substrate of a tRNA splicing endonuclease into an animalia cell, wherein the substrate is labeled at the 5' end with a fluorophore and at the 3' end with a quencher;

(b) contacting the cell with a member of a library of compounds; and

(c) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if a fluorescent signal is not detectable or decreased in the presence of the compound relative to the absence of the compound or the presence of a control.

6. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting an animalia cell containing a substrate of a tRNA splicing endonuclease with a member of a library of compounds, wherein the substrate is labeled at the 5' end with a fluorophore and at the 3' end with a quencher; and

(b) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if a fluorescent signal is not detectable or decreased in the

presence of the compound relative to the absence of the compound or the presence of a control.

7. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) microinjecting a substrate of a tRNA splicing endonuclease into a animalia cell, wherein said substrate is labeled at the 5' end with a fluorescent donor moiety and labeled at the 3' end with a fluorescent acceptor moiety;

(b) contacting the cell with a member of a library of compounds; and

(c) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is increased relative to the absence of the compound or the presence of a control.

8. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) transfecting a substrate of a tRNA splicing endonuclease into a animalia cell, wherein said substrate is labeled at the 5' end with a fluorescent donor moiety and labeled at the 3' end with a fluorescent acceptor moiety;

(b) contacting the cell with a member of a library of compounds; and

(c) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is increased relative to the absence of the compound or the presence of a control.

9. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting an animalia cell containing substrate of a tRNA splicing endonuclease with a member of a library of compounds, wherein said

substrate is labeled at the 5' end with a fluorescent donor moiety and labeled at the 3' end with a fluorescent acceptor moiety; and

(b) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is increased relative to the absence of the compound or the presence of a control.

10. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting an animalia cell-free extract with a substrate of a tRNA splicing endonuclease and a member of a library of compounds, wherein the substrate is labeled at the 5' end with a fluorophore and at the 3' end with a quencher; and

(b) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if a fluorescent signal is not detectable or decreased in the presence of the compound is decreased relative to the absence of the compound or the presence of a control.

11. A method of identifying an antiproliferative compound that inhibits or reduces animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting an animalia cell-free extract with a substrate of a tRNA splicing endonuclease and a member of a library of compounds, wherein said substrate is labeled at the 5' end with a fluorescent donor moiety and labeled at the 3' end with a fluorescent acceptor moiety; and

(b) measuring the activity of the tRNA splicing endonuclease, wherein an antiproliferative compound that inhibits or reduces tRNA splicing activity is identified if the fluorescence emission of the fluorescent acceptor moiety at the wavelength of the fluorescent donor moiety in the presence of the compound is increased relative to the absence of the compound or the presence of a control.

12. The method of claim 1, 2 or 3, wherein the compound inhibits tRNA splicing endonuclease activity.

13. The method of claim 1, 2 or 3, wherein the compound enhances tRNA splicing endonuclease activity.

14. The method of any one of claims 1-11, wherein the method further comprises determining the structure of the compound that modulates tRNA splicing endonuclease activity.

15. The method of claim 1, 2, or 3, wherein the reporter gene encodes firefly luciferase, renilla luciferase, click beetle luciferase, green fluorescent protein, yellow fluorescent protein, red fluorescent protein, cyan fluorescent protein, blue fluorescent protein, beta-galactosidase, beta-glucoronidase, beta-lactamase, chloramphenicol acetyltransferase, or alkaline phosphatase.

16. The method of claim 1 or 3, wherein the cell is selected from the group consisting of 293T, HeLa, MCF7, Wi-38, SkBr3, Jurkat, CEM, THP1, 3T3, and Raw264.7 cells.

17 The method of claim 2, 10 or 11, wherein the cell-free extract is a cell extract.

18. The method of any one of claims 1-11, wherein the compound is selected from a combinatorial library of compounds comprising peptoids; random biooligomers; diversomers such as hydantoins, benzodiazepines and dipeptides; vinylogous polypeptides; nonpeptidal peptidomimetics; oligocarbamates; peptidyl phosphonates; peptide nucleic acid libraries; antibody libraries; carbohydrate libraries; and small organic molecule libraries.

19. The method of claim 18, wherein the small organic molecule libraries are libraries of benzodiazepines, isoprenoids, thiazolidinones, metathiazanones, pyrrolidines, morpholino compounds, or diazepindiones.

20. The method of claim 1 or 3, wherein the step of contacting a library of compounds with a cell is in an aqueous solution comprising a buffer and a combination of salts.

21. The method of claim 20, wherein the aqueous solution approximates or mimics physiologic conditions.

22. The method of claim 20, wherein the aqueous solution further comprises a detergent or a surfactant.

23. The method of claim 14, wherein the structure of the compound is determined by mass spectroscopy, NMR, vibrational spectroscopy, or X-ray crystallography.

24. The method of any one of claims 1-11, wherein the compound directly binds the tRNA splicing endonuclease.

25. The method of claim 1, 2 or 3, wherein the compound binds to an RNA transcribed from said reporter gene.

26. The method of claim 4, 5, 6, 7, 8, 9, 10 or 11, wherein the compound binds to the substrate.

27. The method of claim 1, 2 or 3, wherein the compound binds the tRNA intron.

28. The method of any one of claims 1-11, wherein the compound disrupts an interaction between the tRNA and the tRNA splicing endonuclease.

29. The method of claim 1, 2 or 3, wherein the compound disrupts an interaction between the tRNA intron and the tRNA splicing endonuclease.

30. The method of claim 1 or 3, wherein said cell is stably transfected with said nucleic acid.

31. The method of claim 1 or 3, wherein said cell is transiently transfected with said nucleic acid.

32. The method of claim 1 or 3, wherein said cell is transfected with an episomal expression vector comprising said nucleic acid.

33. A method of preventing, treating, managing or ameliorating a proliferative disorder or a symptom thereof, said method comprising administering to a subject in need thereof a therapeutically or prophylactically effective amount of a compound, or a pharmaceutically acceptable salt thereof, identified according to the method of claim 12.

34. A method of preventing, treating, managing or ameliorating a proliferative disorder or a symptom thereof, said method comprising administering to a subject in need thereof an effective amount of a compound, or a pharmaceutically acceptable salt thereof, identified according to the method of claim 12, wherein said effective amount decreases the activity of tRNA splicing endonuclease.

35. The method of claim 33 or 34, wherein the proliferative disorder is cancer.

36. A method of preventing, treating, managing or ameliorating a proliferative disorder or a symptom thereof, said method comprising administering to a subject in need thereof a therapeutically or prophylactically effective amount of an antiproliferative compound or a pharmaceutically acceptable salt thereof, identified according to the method of claim 4, 5, 6, 7, 8, 9, 10 or 11.

37. A method of preventing, treating, managing or ameliorating a proliferative disorder or a symptom thereof, said method comprising administering to a subject in need thereof an effective amount of an antiproliferative compound or a pharmaceutically acceptable salt thereof, identified according to the method of claim 4, 5, 6, 7, 8, 10 or 11, wherein said effective amount decreases the activity of tRNA splicing endonuclease.

38. The method of claim 36, wherein the proliferative disorder is cancer.

39. The method of claim 37, wherein the proliferative disorder is cancer.

40. A method of identifying a therapeutic agent for the treatment or prevention of cancer, or amelioration of a symptom thereof, said method comprising:

(a) contacting a member of a library of compounds with a cell containing a nucleic acid comprising a reporter gene, wherein the reporter gene comprises a tRNA intron; and

(b) detecting the expression of said reporter gene,

wherein if a compound that reduces the expression of said reporter gene relative to the expression of said reporter gene in the absence of said compound or the presence of a control is detected in (b), then

(c) contacting the compound with a cancer cell or a neoplastic cell and detecting the proliferation of said cancer cell or neoplastic cell,

so that if the compound reduces or inhibits the proliferation of the cancer cell or neoplastic cell, the compound is identified as an antiproliferative compound.

41. The method of claim 40 further comprising (d) testing said compound in an animal model for cancer, wherein said testing comprises administering said compound to said animal model and verifying that the compound is effective in reducing the proliferation or spread of cancer cells in said animal model.

42. A method for verifying the ability of a compound to inhibit animalia tRNA splicing endonuclease activity, said method comprising:

(a) expressing a nucleic acid comprising a reporter gene in a cell, wherein the reporter gene comprises a tRNA intron;

(b) contacting said cell with a compound; and

(c) detecting the expression of said reporter gene, wherein a compound that inhibits tRNA splicing endonuclease activity is verified if the expression of said reporter gene in the presence of a compound is reduced as compared to the expression of said reporter gene in the absence of said compound or the presence of a control.

43. A method for verifying the ability of a compound to inhibit animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting a compound with a cell-free extract and a nucleic acid comprising a reporter gene, wherein the reporter gene comprises a tRNA intron; and

(b) detecting the expression of said reporter gene, wherein a compound that inhibits tRNA splicing endonuclease activity is verified if the expression of said reporter gene in the presence of a compound is reduced as compared to the expression of said reporter gene in the absence of said compound or the presence of a control.

44. A method for verifying the ability of a compound to inhibit animalia tRNA splicing endonuclease activity, said method comprising:

(a) contacting a member of a library of compounds with a cell containing a nucleic acid comprising a reporter gene, wherein the reporter gene comprises a tRNA intron; and

(b) detecting the expression of said reporter gene, wherein a compound that inhibits tRNA splicing endonuclease activity is verified if the expression of said reporter gene in the presence of a compound is reduced as compared to the expression of said reporter gene in the absence of said compound or the presence of a control.

45. The method of claim 4, 5, 6, 7, 8, 9, 10 or 11, wherein the substrate comprises a mature domain.

46. The method of claim 1, 4, 5, 7 or 8, wherein said method further comprises: (d) determining the cytotoxic activity of the compound.

47. The method of claim 2, 3, 6, 9, 10 or 11, wherein said method further comprises: (c) determining the cytotoxic activity of the compound.

48. The method of claim 1, 4, 5, 7 or 8, wherein said method further comprises: (d) determining the cytostatic activity of the compound.

49. The method of claim 2, 3, 6, 9, 10 or 11, wherein said method further comprises: (c) determining the cytostatic activity of the compound.

50. The method of claim 1, 4, 5, 7 or 8, wherein said method further comprises: (d) measuring the effect of the compound on yeast tRNA splicing endonuclease.

51. The method of claim 2, 3, 6, 9, 10 or 11, wherein said method further comprises: (c) measuring the effect of the compound on yeast tRNA splicing endonuclease.

52. The method of claim 33 or 34, wherein the subject is a human.

5

53. The method of claim 36, wherein the subject is a human.

54. The method of claim 37, wherein the subject is a human.